

CLAIMS

1. A neuropilin binder (NPB) wherein the NPB is a polypeptide, antibody, scFv, antibody fragment or bioconjugate and is characterized in modulating neuropilin-1 (NP-1) function or having the capability to inhibit NP-1 dependent angiogenesis of endothelial cells and/or invasion of tumor cells, whereby the NPB binds to NP-1 and modulates NP-1 function.
2. The NPB according to claim 1 comprising a sequence selected from the group consisting of SEQ ID No: 1 or SEQ ID No: 2.
3. The NPB according to claim 1 comprising a sequence selected from the group consisting of sequences SEQ ID No: 5 to SEQ ID No: 38.
4. The NPB according to claim 3, whereby the NPB is not binding, interfering or inhibiting the VEGF/neuropilin-1 interaction.
5. The NPB according to claim 1, wherein the NPB is a polypeptide, antibody, scFv, antibody fragment or bioconjugate comprising one CDR3 (Complementary Determining Regions 3) having at least one of the sequences selected from SEQ ID No: 73 to SEQ ID No: 108.
6. The NPB according to any of claims 1 to 5, wherein said NPB is labeled with a detectable label; in particular wherein said detectable label is selected from the group consisting of a radioisotope, an enzyme and a chromophore.
7. Use of the NPB according to any of claims 1 to 6 for the detection of neuropilin-1 expression.
8. Use of the NPB according to any of claims 1 to 6 for the modulation of neuropilin-1 function, particularly modulation or inhibition of neuropilin-dependent invasion or adhesion of cells, preferably tumor cells.

9. A diagnostic kit comprising the NPB according to any of claims 1 to 6 and a container.
10. A composition comprising the NPB according to any of claims 1 to 6 and a pharmaceutical acceptable carrier.
11. An isolated nucleic acid molecule encoding the NPB according to any of claims 1 to 6.
12. A vector comprising a nucleic acid according to claim 11.
13. Use of the NPB according to any of claims 1 to 6 in the manufacture of a medicament for the treatment or prevention of neuropilin-dependent angiogenesis and non-physiological blood vessel growth, particularly correlated with a tumor.
14. Use of the NPB according to any of claims 1 to 6 in the manufacture of a medicament for the treatment or prevention of cancer and/or metastasis of tumor cells, wherein the metastatic potential depends on neuropilin-1-related invasion and/or adhesion, preferably wherein the tumor cells are tumor cells derived from mesodermal cells.
15. The use of claims 13 or 14 wherein the NPB inhibits the function of expressed neuropilin-1, in particular wherein the molecule binds to the extracellular region of neuropilin-1.
16. An *ex vivo* method of determining the dependency of the invasiveness of a naturally occurring invasive cancer cell on the functionality of neuropilin-1, comprising the steps of:
 - b) contacting the cancer cell with a molecule inhibiting neuropilin-1 function;
 - c) contacting said cancer cell with a gel-like matrix under conditions suitable for the growth of said cancer cells; and
 - d) determining the migration of said cancer cells through the gel-like matrix.

17. An *ex vivo* method of determining the dependency of the adhesiveness of a naturally occurring invasive cancer cell on the functionality of neuropilin-1, comprising the steps of:
 - a) contacting the cancer cell with a molecule inhibiting neuropilin-1 function;
 - b) contacting said cancer cell with a layer of extracellular matrix (ECM) proteins under conditions suitable for the growth of said cancer cells; and
 - c) determining the adhesion of said cancer cells to the layer of ECM proteins.
18. The method of claim 17, wherein the layer of ECM proteins comprises one protein selected from the group consisting of collagen S type I, collagen VI, fibronectin, laminin, nidogen, entactin, and vitronectin.
19. A method of identifying a ligand binding specifically to the extracellular region of neuropilin-1, wherein said ligand is capable of inhibiting angiogenesis, tube formation of endothelial cells, and/or invasion or adhesion of tumor cells, comprising the steps of:
 - a) contacting a phage library of ligands with cancer cells or endothelial cells;
 - b) isolating said cells;
 - c) removing phages bound unspecifically and/or not bound to said cells;
 - d) eluting phages bound to said cells; and optionally
 - e) determining the identity of the ligand represented by said binding to neuropilin-1
 - f) testing the ligand in biochemical or biological assays on its capability to interfere with NP-1 function.
20. The method of claim 19, instead of steps e) further comprising the steps of:
 - e) contacting eluted phages with immobilized NP-1;

- 75 -

- f) washing said NP-1 with detergent and/or high salt;
- g) eluting phages bound to NP-1; and
- h) determining the identity of the ligand represented by said eluted phages.

21. A method of treating or preventing cancer or metastasis in a patient, said method comprising administering to said patient the NBP according to any of claims 1 to 6, the composition according to claim 10, the nucleic acid sequence according to claim 11 or a ligand identifiable by the method of claims 19 or 20 in an amount effective to inhibit metastasis of neuropilin-1 mediated invasion and/or adhesion.

22. A method of treating or preventing cancer or metastasis in a patient, said method comprising administering to said patient the NBP according to any of the claims 1 to 6, the composition according to claim 10, the nucleic acid sequence according to claim 11 or a ligand identifiable by the method of claims 19 or 20 in an amount effective to inhibit tumor-associated, neuropilin-dependent angiogenesis.